I. GENETICS

TRISOMY 18 AND AGENESIS OF CORPUS CALLOSUM: A CASE REPORT

Valerica Belengeanu[1], Marioara Boia[1], Gabriela Diaconescu[2], Nicoleta Andreescu[1], Simona Farcas[1], Monica Stoian[1]

[1] University of Medicine and Pharmacy "V. Babes" of Timisoara

[2] Clincal Hospital No. 1, Timisoara, Neonatology Department

Abstract

Trisomy 18 syndrome is caused by the presence of an extra number 18 chromosome, which leads to multiple abnormalities. Many of these malformations make it hard for infants to live longer than a few months. We present a case of trisomy 18 with agenesis of corpus callosum in a newborn male with intrauterine growth retardation that was investigated for growth retardation and facial dismorphy. The cytogenetic analysis revealed a complete trisomy 18 karyotype.

Key words: trisomy 18, multiple abnormalities

Introduction

Edwards et al. and Smith et al. first described trisomy 18 separately in 1960. Edwards syndrome or complete trisomy 18, is the second most common autosomal trisomy in newborns, after Down syndrome, with a prevalence at birth of about 1 in 6000 [Root and Carey, 1994]. It is a chromosomal disorder that was widely described resulting from three copies of the chromosome 18 in every cell. The additional chromosome 18 usually results from maternal non-disjunction in 90% of the cases and of paternal non-disjunction in 10% of the cases. The affected patients manifest multiple congenital malformations, mental retardation, feeding difficulties, developmental delays. Surviving rate is very low about 55-65% of newborns with trisomy 18 die in the first week of life, and 90% have died by 6 months of age and only about 5-10% of infants are alive at 1 year of age [Root and Carey, 1994]. Children born at term and females have a better surviving rate than premature births and males [Niedrist et. al., 2006].

Case report

The proband (Fig.1, Fig 2) a newborn male is the second child of a healthy couple. Mother's age at birth was 30 years and father's was 38 years. The newborn had intrauterine growth retardation, he weight at birth 2330 g, head circumference was 31 cm, length: 48 cm and thoracic circumference: 31 cm. Ultrasonographic examination was performed during pregnancy but no worrying signs were found therefore antenatal screening was not completed.

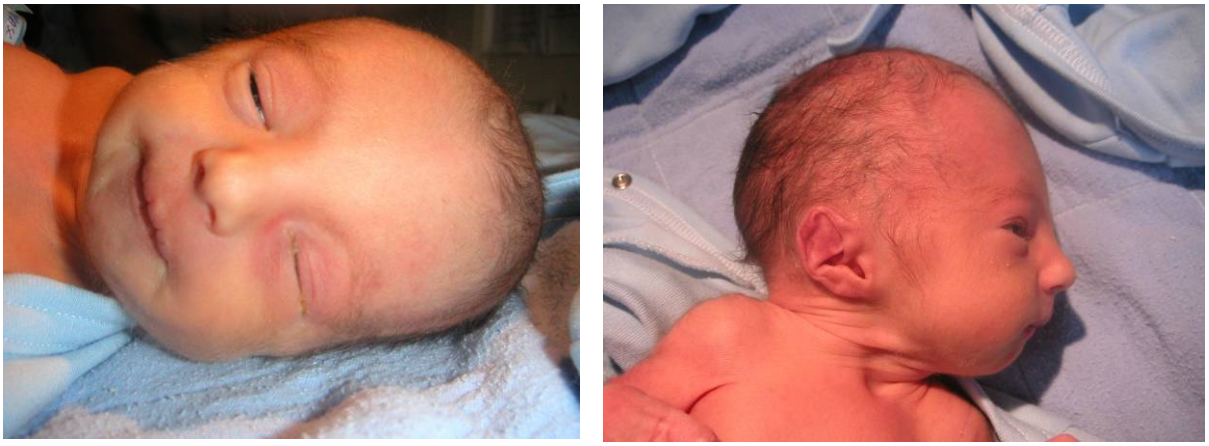

Fig.1, Fig 2. The male newborn – the second child of a healthy couple.

The proband was investigated at birth for growth retardation and facial dismorphy. On examination the following anomalies were observed: microcephaly, ocular hypertelorism, short palpebral fissures, microstomia, micrognathia, low set, malformed ears, arthrogryposis, clenched hands with the index finger overriding the middle finger and the fifth finger overriding the fourth finger, rocker-bottom feet. The newborn showed signs of neonatal hypotonia.

Brain ultrasonography was performed and the pathological findings were: minor enlargement of posterior hornes of the lateral ventricles and agenesis of corpus callosum.

Cardiac system was investigated, and the physical examination with a stethoscope revealed a heart murmur and at the transthoracic echocardiogram a ventricular septal defect was discovered.

Renal ultrasonography was also a part of the investigations, as the anomalies of this system are known to be frequent, but no signs of renal malformations were revealed.

Cytogenetics

Chromosome analysis from peripheral blood lymphocytes was performed. A total of 50 metaphases were counted and in all cells a supernumerary chromosome 18 was present. Thus the chromosomal investigation revealed a complete trisomy 18; the karyotype was 47,XY,+18 (Fig.3, Fig. 4).

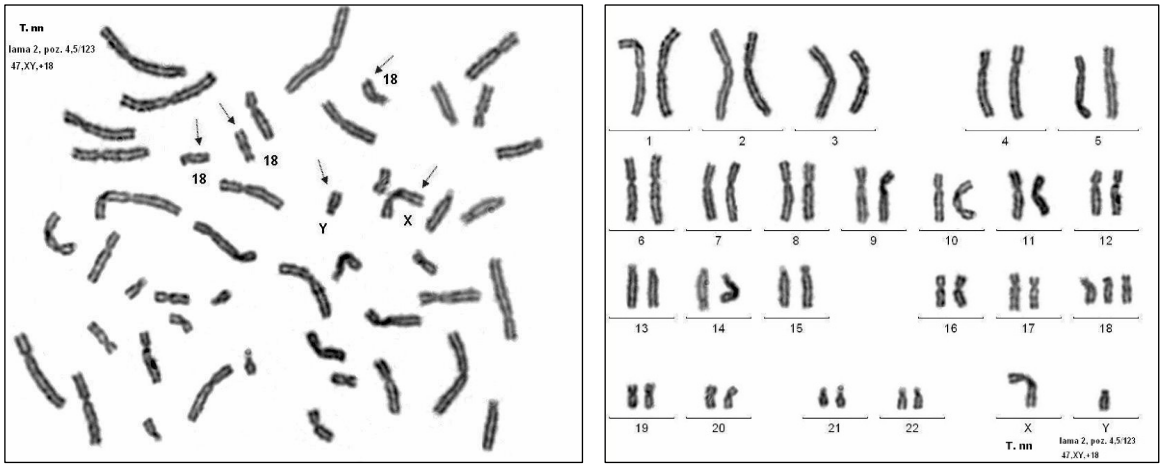

Fig.3, Fig. 4. Complete trisomy 18; the karyotype was 47,XY,+18.

Discussions

The phenotypical appearance of our patient was suggestive for trisomy 18 as the informative findings for this syndrome were present. The patient anomalies that are found in more than 50% of the trisomy 18 cases are: intrauterine growth retardation, short palpebral fissures, microstomia, micrognathia, prominent occiput, low-set, malformed ears, short neck with excessive skin folds, clenched hand, crossed fingers, hypoplasia of toe nails, short dorsiflexed hallux, rocker-bottom feet, mild hirsutism of the forehead and back, neonatal hypotonia. Anomalies present in 10-50% of the cases are microcephaly, foot valgus. Agenesis of corpus callosum is one of the less common findings in trisomy 18 cases. It is known to be present as associated malformation in less than 10% of the cases and among the CNS malformations is very infrequent also [Case et al. 1977].

The cytogenetic analysis made certain the phenotypical suspicion for trisomy 18. The karyotype was of a complete trisomy (47,XY,+18). There have been described in the literature cases of mosaic trisomy 18, partial trisomy 18 (18p, 18q) and even double aneuploydies, three copies of chromosome 18 and an extra 21, X or Y chromosome in the same cell. Complete trisomy 18 results from meiotic non-disjunction, which is in 90% cases maternal. More recent studies have provided the information that in contrast to Down syndrome and Patau syndrome, in Edwards syndrome meiosis II non-disjunction prevails. Baty et al. have concluded in a study that the risk for trisomy 18 after the occurrence of one case with free trisomy is about 0.5%.

Survival of the patient with trisomy 18 is very short as most of the affected children die within the first year of life. There has been little documentation of the precise reason for death in infants with trisomy 18 [Carey, 2001]. The most frequent cause of death in newborn period cited in the literature was sudden cardiac or cardiopulmonary arrest, but all of the patients had congenital heart malformations. Later on the main causes of death are aspiration pneumonia, seizures, cardiac and renal failure.

In conclusion because trisomy18 is not absolutely fatal, our patient must be followed in evolution to establish the possible complication and the prognosis advitam.

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Correspondence to:

Valerica Belengeanu,
Genetics,
University of Medicine and Pharmacy "V. Babes" Timisoara
P-ta Eftimie Murgu nr. 2,
Timisoara
Romania